03-1328
(Serial No. 08/485,129)

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

IN RE DAVID WALLACH, HARTMUT ENGELMANN,
DAN ADERKA, DANIELA NOVICK, and MENACHEM RUBINSTEIN

Appeal from the United States Patent and Trademark Office, Board of Patent Appeals and Interferences

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BRIEF FOR APPELLANTS

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CERTIFICATE OF INTEREST

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

IN RE WALLACH v. _____

No. 03-1327

Certificate of Interest

Counsel for the ~~(petitioner)~~ (appellant) ~~(cross-appellant) (respondent) (appellee) (amicus) (name of party)~~

Wallach et al certifies the following (use "None" if applicable; use extra sheets if necessary):

1. The full name of every party or amicus represented by me is:

David Wallach, Hartmut Engelmann, Dan Aderka, Daniela Novick and Menachem Rubinstein

2. The name of the real party in interest (if the party named in the caption is not the real party in interest) represented by me is:

Yeda Research and Development Co. Ltd.

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or amicus curiae represented by me are:

None

4. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in this court are:

None

April 24, 2003
Date

Signature of counsel

Roger L. Browdy
Printed name of counsel

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I. STATEMENT OF RELATED CASES

No other appeal in or from the same proceeding in the U.S. Patent and Trademark Office was previously before the Federal Circuit or any other appellate court.

It is not believed that any case is pending in this or any other court that will directly affect or be directly affected by this court's decision in the pending appeal. The patent application, the rejection of which is the subject of the present appeal, is a divisional of parent application 07/930,443, filed August 19, 1992. All of the claims in the present case are drawn to invention(s) deleted from the parent application in light of a restriction requirement. The claims remaining in said parent application, drawn to the TBP-II protein, are now involved in an interference proceeding with the claims of U.S. patent 5,344,915. This is pending Interference No. 103,625, under the name *LeMaire v. Wallach.* A final decision has been rendered by the Board of Patent Appeals and Interferences, which decision is currently on appeal to the United States District Court for the District of Columbia, under the name *Goliath Hundertzehnte Vermoegensverwaltungs-Gesellschaft mbH v. Yeda Research and Development Co. Ltd.*, Case No. 00-1720RMU. While it is not believed that this interference will directly affect or be directly affected by or have a bearing on this court's decision in the present appeal, it is nevertheless being brought to this court's attention as it is related in the sense discussed above.

II. JURISDICTIONAL STATEMENT

(a) The Board of Patent Appeals and Interferences had jurisdiction below under 35 U.S.C. §134.

(b) This court has jurisdiction under 35 U.S.C. §141 and 28 U.S.C. §1295(a)(4)(A).

(c) The decision appealed from was issued on December 26, 2002. Notice of Appeal was filed by appellant Wallach et al on February 26, 2003. Thus, the appeal was timely because it was filed within two months of the decision pursuant to 35 U.S.C. §142 and 37 C.F.R. §1.304(a).

(d) Appellant asserts that this appeal comes from a final order of the Board of Patent Appeals and Interferences that disposes of all of appellant's claims in the underlying application.

III. STATEMENT OF ISSUES PRESENTED FOR REVIEW

The following issue is presented in this appeal:[1]

Is there adequate written description for a claim covering all DNA sequences that encode a novel isolated protein defined by a partial amino acid sequence and other characterizing features?

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[1] Additional issues were before the Board below, but as the Board found its disposition of the issue pending in this appeal to be dispositive, the Board found it unnecessary to discuss the additional issues. If, as a result of the present appeal, this court reverses the decision of the Board below, it is requested that this case be remanded to the Board for consideration and disposition of the remaining issues that had been before it but were not decided.

IV. BRIEF STATEMENT OF THE CASE

The patent application under appeal stems from a decision by the Board of Patent Appeals and Interferences (the "Board") of the U.S. Patent and Trademark Office (the "PTO") sustaining a rejection of the examiner of claims 11-13, 35-38, 43, 44, 46-49, 51-54, 56-61, 63 and 64. The only rejection decided by the Board and the sole rejection here on appeal is the unpatentability of the claimed invention under the written description requirement of the first paragraph of 35 U.S.C. §112.

The patent application under appeal involves the discovery of the present inventors of tumor necrosis factor (TNF) binding protein II (TBP-II) (A19[2]), which was initially isolated from human urine and was found to have the ability to selectively inhibit the cytotoxic effect of TNF (A24-25). Under certain conditions it can also act as a carrier for TNF and, thus, prolong its beneficial effects (A24 and A51-60). This naturally-occurring TBP-II, which was isolated from the urine, was found to include the following partial amino acid sequence: Thr-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr in the portion of the protein sequenced by N-terminal sequence analysis (A25). This

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[2] Reference to the appendix will be by reference to the appendix page numbers with the prefix "A". Reference to portions of the decision below will be cited by reference to the applicable appendix page number. The same page numbers are used in the copy of the decision below attached hereto as Addendum A. Reference to the papers from parent application 07/930,443, attached hereto as Addendum B, will be cited by "Add. B", followed by the page number.

TBP-II derived from human urine concentrate showed an apparent molecular weight of 30 kD in reducing SDS-PAGE analysis (A25).

The claims which are on appeal before this court are directed to isolated DNA molecules that encode the newly-discovered TBP-II protein and active fragments thereof, as well as replicable expression vehicles containing such DNA, host cells transformed with the replicable expression vehicle, and processes for producing TBP-II by culturing such a transformant host cell (A330-337).

V. STATEMENT OF THE FACTS

1. A complete copy of all of the claims on appeal appears in the Appendix (A330-337). Claim 11 was considered by the Board as being illustrative of the subject matter on appeal and reads as follows (A330):

> 11. An isolated DNA molecule comprising a contiguous nucleotide sequence coding for a protein consisting of naturally occurring human Tumor Necrosis Factor (TNF) Binding Protein II, herein designated TBP-II, said TBP-II including the amino acid sequence: Thr-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr in the portion of the protein sequenced by N-terminal sequence analysis, said protein having the ability to inhibit the cytotoxic effect of TNF, wherein said naturally occurring TBP-II protein is the same as that protein having the ability to inhibit the cytotoxic effect of TNF which, after being purified by subjecting a crude protein recovered from a dialyzed concentrate of human urine to affinity chromatography on a column of immobilized TNF, elutes from a reversed-phase high pressure liquid chromatography column as a single peak in a fraction corresponding to about 31% acetonitrile and shows a molecular weight of about 30 kDa when measured by SDS-PAGE under reducing conditions.

2. For the purpose of the sole issue involved in this appeal, all of the remaining claims may be considered to stand or fall with the allowability of claim 11.

3. The claimed isolated DNA molecule is a contiguous nucleotide sequence coding for a protein designated TBP-II, defined by ten amino acids in the portion of the protein sequenced by N-terminal sequence analysis, having the ability to inhibit the cytotoxic effect of TNF, which is the same TBP-II that naturally occurs in the urine and may be purified from urine by a series of steps as specified in the claim to yield a protein having a molecular weight of about 30 kD when measured by SDS-PAGE under reducing conditions.

4. The written description of the present specification includes the following passage at page 8, lines 20-23 (A26):

> Thus the invention concerns DNA molecules comprising the nucleotide sequence coding for TBP-II or for a protein substantially homologous therewith. These DNA molecules may be genomic DNA, cDNA, synthetic DNA and combinations thereof.

5. The written description of the present application includes the language of claim 11 as originally filed,[3] which states (A57):

> 11. A DNA molecule comprising the nucleotide sequence coding for the TNF Binding Protein TBP-II of claim 1 or to a protein homolog therewith.

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[3] Original claims constitute their own description; *In re Koller*, 613 F.2d 819 (CCPA 1980).

6. The written description of the present specification at page 10, lines 13-19, reads (A28):

> Once one or more suitable peptide fragments have been sequenced or a partial sequence of the protein is determined, the DNA sequences capable of encoding them are examined. Due to the degeneration of the genetic code, more than one codon may be used to encode a particular amino acid and one or more different oligonucleotides can be produced, each of which would be capable of encoding the TBP-II peptide fragments (Watson, J.D., in: Molecular Biology of the Gene, 3rd ed., W.A. Benjamin, Inc. Menlo Park, CA (1977), pp,. 356-357).

7. The genetic code, referred to in the last quoted portion of the specification, appears at page 356 of the Watson publication cited therein as Table 13-7 (A358), which table is repeated here:

Table 13-7 The Genetic Code

First Position (5' End)	Second Position				Third Position (3' End)
	U	C	A	G	
U	Phe	Ser	Tyr	Cys	U
	Phe	Ser	Tyr	Cys	C
	Leu	Ser	Term[a]	Term	A
	Leu	Ser	Term	Trp	G
C	Leu	Pro	His	Arg	U
	Leu	Pro	His	Arg	C
	Leu	Pro	GluN	Arg	A
	Leu	Pro	GluN	Arg	G
A	Ileu	Thr	AspN	Ser	U
	Ileu	Thr	AspN	Ser	C
	Ileu	Thr	Lys	Arg	A
	Met	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	U
	Val	Ala	Asp	Gly	C
	Val	Ala	Glu	Gly	A
	Val	Ala	Glu	Gly	G

[a] Chain terminating (formerly called "nonsense").

8. From the genetic code referred to in the above-quoted portion of the present specification and the sequence set forth in claim 11, one of ordinary skill in the art could readily determine that the nucleotide sequence encoding said ten amino acids must be the following:

Thr-Pro-Tyr-Ala-Pro-Glu-Pro-Gly- Ser -Thr

ACN-CCN-UAY-GCN-CCN-GAR-CCN-GGN-(UCN or AGY)-ACN

where N is A or G or C or U; Y is U or C; and R is G or A.[4]

9. At page 8, lines 4-5, and 10-11 (A354), and page 9, line 17 (A355), of the Examiner's Answer, the examiner conceded that "the amino acid sequence of TBP II is an inherent property of said protein."

10. At page 9, lines 11-12 (A355), of the Examiner's Answer, the examiner conceded that "the nucleic acid encoding a protein can be deduced based on the amino acid sequence of a protein."

11. It is now known that urinary TBP-II has a sequence of 185-192 amino acids (A383).

12. The Wallach et al application under appeal herein is a divisional of U.S. application 07/930,443 (A15). Claim 67 of that application has been allowed (Add. B11), on the basis of which that application has been placed into an interference with the claims of U.S. patent 5,344,915 (Add. B7-10). Allowed claim 67 of the parent application reads as follows (Add. B1):

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[4] Nomenclature approved by 37 C.F.R. §1.821(a)(1); see Manual of Patent Examining Procedure ("MPEP") §2422, Table 1, for WIPO Standard ST.25 (1998), Appendix 2, Table 1, incorporated by reference therein.

> 67. An isolated and purified Tumor Necrosis Factor (TNF) binding protein (TBPII) having the following characteristics:
>
> (i) an N-terminal amino acid sequence: Xaa-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr, where Xaa consists of the following amino acid sequences: Thr-Val-Ala-Phe-Thr, and Phe-Thr;
>
> (ii) the ability to inhibit the cytotoxic effect of TNF-α on murine A9 cells;
>
> (iii) a molecular weight of about 30 kd in reducing SDS-PAGE analysis.

Thus, the PTO effectively concedes that the TBP-II protein, which the present isolated DNA encodes, is sufficiently described in the present specification (which is the same specification as the parent application) to comply with the written description requirement of 35 U.S.C. §112.

VI. SUMMARY OF THE ARGUMENT

The decision of the Board that is the subject of this appeal issued before the opinion in *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313 (Fed. Cir. 2003). In *Amgen*, the Court again stated that 35 U.S.C. §112 only requires the court to determine whether the specification conveys to one of ordinary skill in the art as of the filing date, that the inventors invented the claimed subject matter. *Id.* at 1331. Moreover, the case law relied upon by the Board, including *University of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997), was found in *Amgen v. Hoechst* to be readily distinguishable in the fact intensive analysis of the written description requirement.

Here, the specification establishes that the present inventors were in possession of the genus of DNA sequences as set forth in claim 11 at the time the application was filed. Because of the disclosure of a partial amino acid sequence and the incorporation by reference of the well-known genetic code setting forth the corresponding codons for each of the amino acid residues of the partial amino acid sequence, the present specification implicitly sets forth a genus of partial DNA sequences of 30 nucleotides each, each of which encodes the partial amino acid sequence set forth in claim 11. This plurality of partial nucleotide sequences, each of which is a partial sequence of the species of the claimed genus of isolated DNA molecules, in conjunction with the claimed function of encoding the naturally-occurring TBP-II protein, which has been conceded to be adequately described in the present specification, is sufficient to meet the written description requirement for the claimed genus. Just as a partial amino acid sequence combined with other distinguishing characteristics may be sufficient to fingerprint the protein so as to distinguish it from all other proteins, so too does the disclosure of a partial nucleotide sequence, in combination with sufficient other identifying characteristics so as to distinguish it from all other nucleotide sequences, adequately describe a DNA sequence.

Furthermore, the complete amino acid sequence of a protein is an inherent property of an isolated protein which has been fully characterized by partial amino acid sequence and other characteristics. The complete amino acid sequence of a

protein automatically puts one in possession of all DNA sequences encoding it, as the genetic code is based on an unequivocal correspondence between amino acids and encoding DNA codons. Therefore, one who has isolated a novel protein and fully characterized it by partial amino acid sequence and other characteristics, is inherently in possession of the complete amino acid sequence thereof and, thus, also inherently in possession of all DNA sequences encoding that amino acid sequence.

The present specification discloses the isolation of the TBP protein and sets forth sufficient identifying characteristics, including partial amino acid sequence, to establish that the inventors were in possession of that protein, thereby establishing an adequate written description for the TBP-II protein. As appellants have demonstrated possession of the TBP-II protein, appellants were also necessarily in possession of its inherent amino acid sequence, as well as all of the DNA sequences encoding that amino acid sequence. Accordingly, the claimed genus of nucleotide sequences that encode the naturally-occurring TBP-II protein is adequately supported by the written description of the present specification.

VII. ARGUMENT

A. Statement of the Standard of Review

Compliance with the written description requirement is a question of fact. *Enzo Biochem Inc. v. Gen-Probe Inc.*, 296

F.3d 1316, 1323 (Fed. Cir. 2002), *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991). The Board's factual findings are reviewed for substantial evidence, *In re Gartside*, 203 F.3d 1305, 1316 (Fed. Cir. 2000).

B. 35 U.S.C. §112 Does not Mandate the Disclosure of a Complete Contiguous Nucleotide Sequence in Order to Support a Claim Drawn to a DNA Molecule

The written description requirement of 35 U.S.C. §112, first paragraph, is set forth as follows:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person of skill in the art to which it pertains or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

As stated in *Enzo Biochem Inc. v. Gen-Probe Inc.*, *supra*, at 1324:

> Compliance with the written description requirement is essentially a fact-based inquiry that will "necessarily vary depending on the nature of the invention claimed." [*Vas-Cath*, 935 F.2d at 1563, 19 USPQ2d at 1117] (citing *In re DiLeone*, 58 C.C.P.A. 925, 436 F.2d 1404, 1405, 168 USPQ 592, 593 (C.C.P.A. 1971)).

The Board below held in the paragraph bridging pages 5 and 6 of its decision (A5-6):

> Not one species of a contiguous nucleotide sequence, supporting the genus of DNA molecules covered by claim 11, is described in the specification. Where, as here, not one species within the scope of claim 11 is described in the specification, we find that applicants fall short of describing the genus of DNA molecules covered by claim 11. [footnote omitted] Applicants' specification

> does not describe representative examples of DNA molecules within the genus of claim 11.

The Board further held that a functional description of DNA, i.e., coding for TBP-II, is not enough to comply with the statute, citing *Amgen Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991), *Fiers v. Revel*, 984 F.2d 1164, 1170-1171 (Fed. Cir. 1993) and *University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997) (A6-8). Also, although decided after the briefings were filed below, the Board stated that the opinion in *Enzo Biochem Inc. v. Gen-Probe Inc.*, *supra*, is consistent with and adheres to the principles of law enunciated in *Amgen*, *Fiers* and *Eli Lilly* (A9).

However, the Board overlooked the fact that *Enzo* distinguishes *Eli Lilly*. *Enzo* notes that *Eli Lilly* holds that a gene material which has been defined only by a statement of function or result did not adequately describe the claimed invention. However, *Enzo* goes on to say at 1324:

> It is not correct, however, that all functional descriptions of genetic material fail to meet the written description requirement.

The fact that *Enzo* distinguishes *Eli Lilly* and limits it to its facts has been noted in even more recent cases, such as *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306 (Fed. Cir. 2003). Note where it states at 1320:

> Invoking §112, *Lilly* required a precise definition of a DNA sequence in the patent specification. In more recent cases, however, this court has distinguished *Lilly*. For instance, in *Enzo Biochem Inc. v. Genpro, Inc.* [*supra*], neither the specification nor the deposited biological material recited the precise "structure, formula, chemical name, or

physical properties" required by *Lilly*. *Id. at 1324*, (quoting *Lilly*, 119 F.3d at 1566). Although this court initially determined that the specification in *Enzo* did not satisfy the *Lilly* disclosure rule, it revisited the issue and remanded to the district court. The court instructed:

> On remand the court should determine whether a person of skill in the art would glean from the written description, including information obtainable from the deposits of the claimed sequences, subsequences, mutated variants and mixtures sufficient to demonstrate possession of the generic scope of the claims.

Enzo, 296 F.3d at 1328.

Note also *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313 (Fed. Cir. 2003), where it states at 1332:

> More recently, in *Enzo Biochem*, we clarified that *Eli Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.

In *Enzo*, this court adopted the PTO's applicable standard for determining compliance with the written description requirement as set forth in the Guidelines for Examination of Patent Applications under the 35 U.S.C. §112, ¶1, "Written Description" Requirement, 66 Fed. Reg. 1099 (Jan. 5, 2001) ("Guidelines") governing its internal practice for addressing the written description issue, stating at 1324-1325:

> In its Guidelines, the PTO has determined that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ... i.e., complete or partial structure, other physical and/or chemical properties, functional

> characteristics when coupled with a known or disclosed correlation between function and structure or some combination of such characteristics." Guidelines, 66 Fed. Reg. at 1106 .... We are persuaded by the Guidelines on this point and adopt the PTO's applicable standard for determining compliance with the written description requirement.

Here, the Board has ignored appellants' analysis of the specification, establishing disclosure of sufficiently detailed, relevant identifying characteristics, including partial structure and other physical and/or chemical properties and functional characteristics with a known or disclosed correlation between function or structure, and has blindly adhered to the supposed strict requirements of *Amgen, Fiers* and *Eli Lilly*, effectively concluding that a DNA can never be claimed without reciting a complete nucleotide sequence. The Board essentially ruled that there is a higher standard for written description for DNA inventions than for any other invention. Note page 5 of the decision (A5), where it states:

> [R]elevant principles of law enunciated by our reviewing court require that genetic material be supported in the original specification by written description containing a relatively high degree of specificity.

Enzo clarifies, however, that there is no *per se* rule for DNA inventions and all of the specification must be analyzed to determine whether appellants are in possession of the full scope of the claimed invention. Thus, the Board's factual finding of lack of written description is unsupported by substantial evidence.

C. The Present Claims Are Directed to a Genus of DNA Molecules

Claim 11 is directed to any isolated DNA molecule that has a contiguous nucleotide sequence coding for the naturally-occurring human TBP-II protein (SF 1[5]). Because of the degeneracy of the genetic code, a plurality of different nucleotide sequences can encode the same amino acid sequence (SF 7). It is important to understand that only a single protein is encoded by the presently-claimed DNA (SF 3). Thus, the present claims are distinguishable from the claims in the *Eli Lilly* case, in which the patentee was attempting to claim DNA encoding a plurality of proteins, i.e., insulin from a plurality of different species. Here, the claim is only directed to DNA encoding TBP-II from a single species, human. The claim is only generic in the sense that it covers all of the different nucleotide sequences that encode this single protein. As the examiner below conceded, the nucleic acid encoding a protein can be deduced based on the amino acid sequence of a protein (see SF 10). An example of how the nucleotide sequence can be deduced based on an amino acid sequence, reference is made to paragraphs 7 and 8 of the Statement of Facts, where a generic formula for all of the nucleic acid sequences encoding the ten amino acid sequence set forth in claim 11 is deduced and stated.

[5] Reference to the Statement of Facts, hereinabove, will be by citing "SF", followed by the paragraph number.

D. A Partial Sequence and Other Distinguishing Characteristics Is Sufficient to Demonstrate Possession of DNA

In the present specification, a contiguous partial structure of the claimed DNA sequences is implicitly set forth[6], see SF 8. *Enzo* recognizes that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." *Enzo*, *supra*, at 1324, quoting Guidelines, 66 Fed. Reg. at 1106. Thus, the existence of a partial structure is an important factor in determining whether the written description requirement has been met. Besides this partial sequence, claim 11 provides that the DNA molecule encodes the naturally-occurring human TBP-II protein. While this limitation is functional, *Enzo* clarifies that not all functional descriptions of genetic material fail to meet the written description requirement, stating at 1324:

> It is not correct, however, that all functional descriptions of genetic material fail to meet the written description requirement.

Thus, for example, a partial structure, when coupled with a known or disclosed correlation between function and structure,

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[6] See Guidelines, 66 Fed. Reg. at 1107 ("To comply with the written description requirement of 35 U.S.C. §112, ¶1, each claim limitation must be expressly, implicitly, or inherently supported in the originally filed disclosure." [footnotes omitted]).

can be sufficient to satisfy the written description requirement.

Here, the genetic code provides the known correlation between structure and function. The protein, which the DNA of claim 11 encodes, has been admitted by the PTO to have been adequately described in the present specification by partial amino acid sequence combined with sufficient other physical and/or chemical properties so as to adequately characterize or fingerprint that protein (SF 12). This is evidenced by the fact that a claim to that protein has been found to be patentable by the examiner and is now involved in an interference proceeding (Add. B7-10).

It is apparent from the disclosure of the present specification at page 10, lines 13-19 (SF 6), in conjunction with the disclosure of a partial sequence of the protein and the reference to the pages of Watson that contains the genetic code, that the present appellants were able to envision the detailed constitution of a significant portion of the DNA sequence encoding TBP-II, so as to distinguish it from other material (SF 8). This implicit description of a partial sequence of the claimed DNA, including 30 nucleotides, is an important unique bit of characterizing information. This piece of nucleotide structure, in conjunction with the characterizing information that the DNA encodes a protein having the ability to inhibit the cytotoxic effects of TNF, which protein is itself adequately described, provides sufficient relevant identifying characteristics to comply with the criteria of the above-quoted

portion of the Guidelines cited with approval by *Enzo*. This is a disclosure of sufficiently detailed relevant identifying characteristics so as to establish that the invention was complete and the inventors were in possession of the claimed DNA invention.

E. One in Possession of a Novel Protein is Inherently in Possession of All DNA Sequences Encoding the Amino Acid Sequence of that Protein

The complete amino acid sequence of a protein is an inherent property of an isolated protein which has been fully characterized by a partial amino acid sequence and other characteristics. This point has been conceded by the examiner below by statements to that effect in the Examiner's Answer (SF 9). See *University of New Mexico v. Knight*, 321 F.3d 1111, 1122 (Fed. Cir. 2003), citing with approval from *In re Papesch*, 315 F.2d 381, 391 (CCPA 1983):

> From the standpoint of patent law, a compound and all of its properties are inseparable; they are one and the same thing. The graphic formulae, and the chemical nomenclature, the systems of classification and study such as the concepts of homology, isomerism, etc., are mere symbols by which compounds can be identified, classified, and compared.

The same is true for the amino acid sequence of a protein. See also *In re Nathan*, 328 F.2d 1005, 1009 (CCPA 1964), which allowed a correction to the structural formula of a chemical compound, stating that the amendatory material "is concerned with an inherent characteristic of an illustrative product of appellants' invention already sufficiently identified in appellants' original disclosure as filed." Furthermore, in the

Board decision of *Ex parte Deuel*, 27 USPQ2d 1360, 1363 (Bd Pat App & Int 1993), the Board noted the examiner's position that the amino acid sequence is an inherent characteristic of the protein.

Thus, for the purpose of the written description requirement, regardless of whether or not the amino acid sequence of TBP-II was set forth in full in the specification, it is clear that appellants were in possession of that inherent amino acid sequence at the time the application was filed.

The portions of the specification quoted in paragraphs 4-6 of the Statement of Facts, hereinabove, make clear that appellants considered the DNA that encodes the TBP-II amino acid sequence to be part of their invention, including not only the genomic DNA and cDNA, but also synthetic DNA, i.e., any DNA sequence that encodes TBP-II. Further, the present invention incorporates by reference the genetic code (SF 6 and 7).

As appellants stated in the application as filed that they considered such DNA sequence to be part of their invention, and as appellants taught how, using the genetic code, to deduce such sequence from the amino acid sequence of TBP-II, and as the full amino acid sequence (from which the genus of encoding DNA sequences may be deduced) was inherently a part of the present specification, it is as if the nucleotide sequence were fully set forth. Thus, the specification establishes that appellants were in possession of such sequences, thereby satisfying the written description requirement of the first paragraph of 35 U.S.C. §112.

The complete amino acid sequence of TBP-II is an inherent property of that otherwise adequately described protein (SF 9). Because the formula of all DNA that encompass that amino acid sequence is dictated by the genetic code, i.e., is a fixed formula, the DNA sequence is as much an inherent property[7] of the adequately described protein, which has been reduced to practice, as is the complete amino acid sequence thereof. Therefore, there is no actual uncertainty that undermines the specificity of the inventors' idea of the invention, such as would require an actual reduction to practice of a DNA before an applicant can be in possession thereof.

Because of the degeneracy of the genetic code, many DNA sequences will encode the amino acid sequence of TBP-II. However, once the complete amino acid sequence for TBP-II is known, all of the DNA sequences that correspond thereto are also known. It is an undisputed scientific fact that, given the complete amino acid sequence of a protein, coupled with knowledge of the genetic code, one is in possession of the genus of all of the DNA sequences that encode that complete amino acid sequence (SF 10). In *In re Deuel*, 51 F.3d 1552, 1560 (Fed. Cir. 1995), this court noted that, with the aid of a computer, a person of ordinary skill in the art may be able to identify all members of the claimed genus of DNA sequences that encode a complete amino acid sequence. Furthermore, footnote 14 of the Guidelines (66 Fed. Reg. at 1108) explicitly states:

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[7] See footnote 6, *supra*.

> [a] genetic code table would correlate a known amino acid sequence with the genus of coding nucleic acids ....

Appellants' specification indisputably demonstrates that appellants were in possession of the TBP-II protein (SF 12). Anyone of ordinary skill in the art would be in possession of the same protein by repeating the experiments described in the specification. Possession of this protein is as good as possession of a deposited sequence, which *Enzo*, at 1326, states may satisfy the written description requirement with respect to a claimed material.

As the complete amino acid sequence of the protein is an inherent characteristic of the protein (SF 9) and as the formula for DNA that encodes the complete amino acid sequence is a fixed formula determined by the genetic code, such DNA formula is also an inherent characteristic of the adequately described protein.

F. The Combination of Described Attributes Establish that Appellants Had Possession of the Claimed DNA Sequences

It has been shown hereinabove that appellants were in possession of a partial sequence (SF 8), which is a common feature possessed by all members of the claimed genus of DNA sequences that distinguish them from others. At 1328, *Enzo* distinguishes *Eli Lilly* as follows:

> In *Eli Lilly*, the specification and generic claims to all cDNAs encoding for vertebrate or mammalian insulin did not describe the claimed genus because they did not set forth any common features possessed by members of the genus that distinguished them from others. [*Eli Lilly*] at 1568 ....

In contradistinction to the situation in *Eli Lilly*, the present claims set forth a common feature possessed by members of the genus that distinguish them from others, i.e., the partial DNA formula set forth at SF 8. That, combined with the feature of encoding a single novel protein, human TBP-II, which protein is otherwise adequately described so as to satisfy the written description requirement, establishes that the written description requirement has been met. If the protein can be described in this manner, then so should the DNA be able to be described in this manner. There is only one written description requirement for all arts.

Furthermore, claim 11 does not claim a cDNA, which is defined as the reverse transcript of an mRNA. A cDNA has a single sequence and that specific sequence cannot be envisioned until it is obtained. One cannot determine the sequence of the cDNA from the amino acid sequence of the protein it encodes. This fact further distinguishes the present situation from the cases relied upon by the Board below. One is in possession of the DNA presently claimed merely by being in possession of the amino acid sequence of the protein as the full array of sequences encoding that protein in accordance with the rules of the genetic code are encompassed by the claim.

Accordingly, as the present claims describe the claimed genus, including common features possessed by members of the genus that distinguish them from others, in combination with the fact that it encodes a protein that is adequately described in the specification and whose amino acid sequence is an

inherent part thereof, the DNA sequences of the present invention are sufficiently described, either explicitly, implicitly or inherently, in a manner that allows those of ordinary skill in the art to understand that appellants were in possession of the invention. Thus, the written description requirement of the first paragraph of 35 U.S.C. §112 is satisfied.

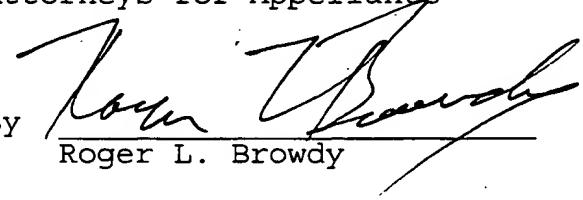
CONCLUSION AND STATEMENT OF RELIEF SOUGHT

For the reasons detailed above, appellants' specification contains a sufficiently detailed written description to allow those of ordinary skill in the art to understand that appellants were in possession of the invention, thus satisfying the written description requirement of the first paragraph of 35 U.S.C. §112.

Accordingly, reversal of the Board and remand for consideration of the remaining issues, which had been briefed but not decided by the Board below, are earnestly solicited.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Appellants

By 
Roger L. Browdy

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PROOF OF SERVICE

I hereby certify that a true copy of the foregoing Motion for Extension of Time and the attached Declaration, Certificate of Interest, and Proposed Order were mailed by depositing with the U.S. Postal Service, with sufficient postage as First Class Mail, addressed to Mary L. Kelly, Esq., Office of the Solicitor, P.O. Box 15667 Arlington, VA 22215, on this 16th day of July, 2003, with a confirmation copy being sent to her by fax on even date.

Roger L. Browdy

CERTIFICATE OF COMPLIANCE

I hereby certify that the present brief complies with the type-volume limitation of FRAP 32(a)(7)(B)(i). The word count of the word processing system used to prepare the brief shows a total of 6110 words, including the Table of Contents, Table of Citations and Statement of Related Cases, as well as this Certificate of Compliance, which need not have been counted in the type-volume limitation. Thus, the portion of the brief which must be counted must contain no more than 14,000 words.

Roger L. Browdy

ADDENDUM A

Paper No. 47

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte DAVID WALLACH,
HARTMUT ENGELMANN,
DAN ADERKA,
DANIELA NOVICK, and
MENACHEM RUBINSTEIN

Appeal No. 2002-1363
Application No. 08/485,129

HEARD: November 21, 2002

Before WINTERS, ADAMS, and GREEN, Administrative Patent Judges.

WINTERS, Administrative Patent Judge.

DECISION ON APPEAL

This appeal was taken from the examiner's decision rejecting claims 11 through 13, 35 through 38, 43, 44, 46 through 49, 51 through 54, 56 through 61, 63, and 64. Claims 14, 39, 45, 50, 55, and 62, which are the only other claims remaining in the

application, stand withdrawn from further consideration by the examiner as directed to a non-elected invention.

The Invention

The invention relates to isolated DNA molecules which encode Tumor Necrosis Factor Binding Protein II (TBP-II). Claim 11, which is illustrative of the subject matter on appeal, reads as follows:

> 11. An isolated DNA molecule comprising a contiguous nucleotide sequence coding for a protein consisting of naturally occurring human Tumor Necrosis Factor (TNF) Binding Protein II, herein designated TBP-II, said TBP-II including the amino acid sequence: Thr-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr in the portion of the protein sequenced by N-terminal sequence analysis, said protein having the ability to inhibit the cytotoxic effect of TNF, wherein said naturally occurring TBP-II protein is the same as that protein having the ability to inhibit the cytotoxic effect of TNF which, after being purified by subjecting a crude protein recovered from a dialyzed concentrate of human urine to affinity chromatography on a column of immobilized TNF, elutes from a reversed-phase high pressure liquid chromatography column as a single peak in a fraction corresponding to about 31% acetonitrile and shows a molecular weight of about 30 kDa when measured by SDS-PAGE under reducing conditions.

The Rejections

In rejecting all of the appealed claims, the examiner does not rely on any prior art references.

Claims 11 through 13, 35 through 38, 43, 44, 46 through 49, 51 through 54, 56 through 61, 63, and 64 stand rejected under 35 U.S.C. § 112, first paragraph, as based on a specification which does not provide an adequate written description of the claimed invention (Paper No. 41, section (10) A). As formatted in the Examiner's

Answer, claims 35 through 38, 43, 44, 46 through 49, and 51 also stand rejected under 35 U.S.C. § 112, first paragraph, on the same ground, i.e., as based on a specification which does not provide an adequate written description of the claimed invention (Paper No. 41, section (10) B). In a sense, the latter "rejection" is subsumed by the former because claims 35 through 38, 43, 44, 46 through 49, and 51 are included in the former rejection based on the same statutory provision. Be that as it may, by entering the latter rejection, the examiner focuses attention on those claims which "read on" a contiguous nucleotide sequence coding for a specified fragment of TBP-II. The examiner offers additional reasons why those claims lack adequate, written descriptive support in the original specification.

In view of our disposition of this appeal, for reasons discussed more fully infra, we find it unnecessary to discuss the separate "rejection" of claims 35 through 38, 43, 44, 46 through 49, and 51 (Paper No. 41, section (10) B). Rather, we confine our discussion to the examiner's rejection of all the appealed claims under 35 U.S.C. § 112, first paragraph, based on a failure to comply with the written description requirement (Paper No. 41, section (10) A).

Deliberations

Our deliberations in this matter have included evaluation and review of the following materials: (1) the instant specification, including all of the claims on appeal; (2) applicants' Appeal Brief (Paper No. 40) and the Reply Brief (Paper No. 42); and (3) the Examiner's Answer (Paper No. 41).

On consideration of the record, including the above-listed mateirals, we affirm the rejection of all the appealed claims under 35 U.S.C. § 112, first paragraph.

Discussion

We first think it prudent to clarify the administrative record with respect to Exhibits A, B, and C attached to applicants' Reply Brief (Paper No. 42). As a general rule, exhibits submitted after the case has been appealed will not be admitted without a showing of good and sufficient reasons why they were not earlier presented. 37 CFR § 1.195 (2001). In this case, however, the examiner did not require a showing under the provisions of Rule 195. Rather, in Paper No. 44, mailed March 13, 2002, the examiner stated that:

> The reply brief filed 2/4/2002 has been entered and considered. The application has been forwarded to the Board of Patent Appeals and Interferences for decision on the appeal.

In our judgment, the only reasonable interpretation which these facts permit is that the examiner (1) waived the provisions of Rule 195; and (2) entered Exhibits A, B, and C, which are attached to and discussed in applicants' Reply Brief. Therefore, we have considered the Reply Brief (Paper No. 42) and the exhibits attached thereto as part of the administrative record. We note in passing that it would have been preferable for the examiner to state explicitly that Exhibits A, B, and C, attached to the Reply Brief, have been admitted and made of record.

In their Appeal Brief (Paper No. 40), page 17, applicants state that "[f]or each rejection, all of the claims grouped for that rejection stand or fall together." In deciding

this appeal, we have focused on the first stated rejection in the Examiner's Answer (Paper No. 41, section (10) A). There, the examiner argues that all of the appealed claims are based on a specification which fails to comply with the written description requirement of 35 U.S.C. § 112, first paragraph. For the purposes of this appeal, we have selected claim 11 from the group of claims under rejection, and we shall decide the appeal on the basis of that claim alone. Accordingly, for the purposes of this appeal, we shall treat all of the appealed claims as standing or falling together with claim 11. See 37 CFR § 1.192(c)(7) (2001). On these facts, we find it unnecessary to discuss the second stated rejection in the Examiner's Answer (Paper No. 41, section (10) B).

We have carefully considered the syllogism set forth in applicants' Appeal Brief and Reply Brief. Although the syllogism is superficially appealing, nevertheless, claim 11 is drawn to genetic material; and relevant principles of law enunciated by our reviewing court require that genetic material be supported in the original specification by a written description containing a relatively high degree of specificity. That is not the case here.

It is not sufficient that applicants contemplate, in their specification, all DNA molecules coding for TBP-II. Applicants acknowledge that the specification does not contain a complete amino acid sequence of TBP-II (Appeal Brief, page 28), much less any specific nucleotide sequence coding for TBP-II. Not one species of a contiguous nucleotide sequence, supporting the genus of DNA molecules covered by claim 11, is described in the specification. Where, as here, not one species within the scope of

claim 11 is described in the specification, we find that applicants fall short of describing the genus of DNA molecules covered by claim 11.[1] Applicants' specification does not describe representative examples of DNA molecules within the genus of claim 11.

In a nutshell, claim 11 is couched in functional terms. Applicants recite an isolated DNA molecule comprising a contiguous nucleotide sequence "coding for" TBP-II. We know what the nucleotide sequence does. In their specification, however, applicants do not describe with a reasonable degree of specificity the structural makeup of even one species of DNA molecule within the scope of claim 11. The claim is generic and couched in functional terms. It is not supported by a specification which provides adequate written descriptive support, with a reasonable degree of specificity, for the claimed DNA. Stated another way, the functional description of DNA in applicants' specification is not enough to comply with the statute. A functional description of DNA does not convey to any person skilled in the art which particular DNA has been invented. Acknowledging the presence of DNA serving a particular function (encoding TBP-II) does not constitute a sufficiently specific written description of any DNA.

As stated in a similar context in Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991):

> A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other

---

[1] The genus of DNA molecules covered by claim 11 includes genomic DNA, cDNA, synthetic DNA, and combinations thereof (specification, page 8).

> materials, and to describe how to obtain it. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, e.g., encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. We hold that when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the gene has been isolated. [citation omitted]

Referring to Amgen, but focusing on the written description requirement of 35 U.S.C. § 112, first paragraph, the court subsequently stated that:

> An adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself. Revel's specification does not do that . . . A bare reference to a DNA with a statement that it can be obtained by reverse transcription is not a description; it does not indicate that Revel was in possession of the DNA. Revel's argument that correspondence between the language of the count and language in the specification is sufficient to satisfy the written description requirement is unpersuasive when none of that language particularly describes the DNA.
>
> As we stated in Amgen and reaffirmed above, such a disclosure just represents a wish, or arguably a plan, for obtaining the DNA. If a conception of a DNA requires a precise definition, such as by structure, formula, chemical name, or physical properties, as we have held, then a description also requires that degree of specificity. To paraphrase the Board [PTO Board of Patent Appeals and Interferences], one cannot describe what one has not conceived. [Fiers v. Revel, 984 F.2d 1164, 1170-1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993); footnote and citation omitted]

Again, in University of California v. Eli Lilly & Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), the court stated that:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. . . .
>
> Thus, as we have previously held, a cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the DNA. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. . . . We will not speculate in what other ways a broad genus of genetic material may be properly described, but it is clear to us, as it was to the district court, that the claimed genera of vertebrate and mammal cDNA are not described by the general language of the '525 patent's written description supported only by the specific nucleotide sequence of rat insulin. [footnote and citations omitted]

Applying those principles of law to the facts before us, we hold that (1) applicants do not describe the genetic material sought to be patented in claim 11 with sufficient specificity in their specification; and (2) the examiner did not err in finding that claim 11

is based on a specification which does not provide adequate, written descriptive support for the claimed subject matter.

Further, in our judgment, the recently issued opinion in Enzo Biochem, Inc. v. Gen-Probe, Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002) is consistent with and adheres to the principles of law enunciated in Amgen, Fiers, and Eli Lilly.[2]

Conclusion

In conclusion, for the reasons set forth in the body of this opinion, we find that claim 11 is based on a specification, as filed, which does not provide adequate, written descriptive support for the claimed subject matter. Accordingly, we affirm the examiner's rejection of claim 11 under 35 U.S.C. § 112, first paragraph (written description requirement). As previously indicated, claims 12, 13, 35 through 38, 43, 44, 46 through 49, 51 through 54, 56 through 61, 63, and 64 fall together with claim 11.

The examiner's decision is affirmed.

---

[2] Enzo Biochem was decided on July 15, 2002, after the briefings were filed in the case before us.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

Sherman D. Winters
Administrative Patent Judge

Donald E. Adams
Administrative Patent Judge

Lora M. Green
Administrative Patent Judge

) BOARD OF PATENT APPEALS AND INTERFERENCES

Browdy and Neimark, P.L.L.C.
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dem

ADDENDUM B

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	Art Unit: 1806
WALLACH et al	)	Examiner: T. Nisbet
Serial No.: 07/930,443	)	Washington, D.C.
Filed: August 19, 1992	)	May 24, 1995
For: TUMOR NECROSIS FACTOR BINDING PROTEIN II, ITS PURIFICATION AND ANTIBODIES THERETO	)	Atty.Docket: WALLACH=5A

AMENDMENT

Honorable Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

Responsive to the Official Action of May 15, 1995, please amend as follows:

IN THE CLAIMS

Insert new claims 67 and 68 as follows:

--67. An isolated and purified Tumor Necrosis Factor (TNF) binding protein (TBPII) having the following characteristics:

i. an N-terminal amino acid sequence: Xaa-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr, where Xaa consists of the following amino acid sequences: Thr, Val-Ala-Phe-Thr-, and Phe-Thr;

ii. the ability to inhibit the cytotoxic effect of TNF-α on murine A9 cells; and

iii. a molecular weight of about 30kd in reducing SDS-PAGE analysis.

68. An isolated and purified Tumor Necrosis Factor (TNF) binding protein (TBPII) having the following characteristics:

i. an N-terminal amino acid sequence: Xaa-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr, where Xaa consists of the following amino acid sequences: Thr, Val-Ala-Phe-Thr-, and Phe-Thr; and

ii. the ability to inhibit the cytotoxic effect of TNF-α on murine A9 cells.--

REMARKS

Claims 33, 34, 36-59 and 62-68 presently appear in this case. While no claims have been allowed, claim 67 has been suggested by the examiner pursuant to 37 C.F.R. §1.605 for the purpose of provoking an interference. MPEP §2305 states that any claim suggested by the examiner "should be the broadest claim within the scope of the prospective count which the applicant's disclosure will support, and which is otherwise patentable to the applicant." Thus, it is apparent that the examiner considers that claim 67 is patentable to the present applicant.

Applicant agrees that claim 67 presented herein, which was proposed by the examiner in the official action of May 15, 1995, is drawn to the same patentable invention as that claimed in patent no. 5,344,915, and therefore an interference should be declared for the reasons set forth in applicant's Request for Interference under 37 C.F.R. §1.607 filed April 5, 1995. In a telephone interview between Examiner Nisbet and the undersigned

attorney, on or about May 2, 1995, after Examiner Nisbet had informally provided the undersigned with a copy of the proposed claim, the examiner advised the undersigned that the language of this proposed claim was selected, at least in part, in order to be fully supported by the disclosure of applicant's first Israeli priority application number 90339, filed May 18, 1989. As MPEP §2308.01 states that when an applicant attempts to provoke an interference with a patent, the examiner must determine the effective filing dates of the application and of the patent, and as the examiner has already made a determination that claim 67 presented herewith has an effective filing date of May 18, 1989, which is earlier than the earliest U.S. filing date of patent no. 5,344,915, it is urged that when the interference is declared, the present applicant must be designated as senior party.

In view of the examiner's statement about claim 67 being entitled to applicant's priority date, it is not necessary to file a declaration under 37 C.F.R. §1.608(a). Nevertheless, out of an abundance of caution, such a declaration is attached hereto.

37 C.F.R §1.605 states:

> At the time the suggested claim is presented, the applicant may also call the examiner's attention to other claims already in the application or presented with the suggested claim and explain why the other claims would be more appropriate to be designated to correspond to a count in any interference which may be declared.

In accordance therewith, applicant hereby calls the examiner's attention to claims 33, 34, 36-41 and 62, which are all believed to be drawn to the same patentable invention, and thus to correspond to any proposed count in any proposed interference.

The same is true with respect to claim 68, presented herewith. It is urged that claim 68 is better suited to be part of the proposed count as it is somewhat broader than claim 67 proposed by the examiner, in eliminating any recitation of molecular weight. It is urged that the molecular weight is not necessary to define the invention in view of the N-terminal amino acid sequence and the other defining information which is present in the claim. Accordingly, it is urged that claim 68 also be designated as corresponding to the count, and, as it is broader than claim 67, that it be used to formulate the count of the proposed interference.

It is noted that the examiner has not complied with the requirement of MPEP §2305.01, which states:

> When an examiner suggests that an applicant present a claim for interference, the examiner should state which of the claims already in the case are, in his or her opinion, unpatentable over the claims suggested. ... If the applicant does present the suggested claim, when the interference is declared, the claims stated to be unpatentable over the suggested claim will be designated as corresponding to the count.

It is urged that all of claims 33, 34, 36-41, 62, 67 and 68 be designated as corresponding to the count. This can be done regardless of the examiner's opinion as to their patentability.

As the examiner considers claim 67 to be patentable to applicant and to be entitled to the effective filing date of May 18, 1989, and as applicant has copied the claim proposed by the examiner verbatim, it is urged that an interference be declared for the reasons set forth in applicants' request of April 5, 1995, and that claims 33, 34, 36-41, 62, 67 and 68 be designated as

corresponding to the count. It is urged that the proposed count of the interference be as set forth in applicants' request of April 5, 1995. Alternatively, it is urged that the proposed count be formulated as follows, based on claim 68 presented herein:

> A purified and isolated TNFα-binding protein which has a molecular weight of about 42,000 daltons and has at the N terminus the amino acid sequence
>
> Xaa Thr Pro Tyr Ala Pro Glu Pro Gly Ser
> Thr Cys Arg Leu Arg Glu
>
> where Xaa is hydrogen, a phenylalanine residue (Phe) or the amino acid sequences Ala Phe, Val Ala Phe, Gln Val Ala Phe, Ala Gln Val Ala Phe, Pro Ala Gln Val Ala Phe or Leu Pro Ala Gln Val Ala Phe
> or
> an isolated and purified Tumor Necrosis Factor (TNF) binding protein (TBPII) having the following characteristics:
> i. an N-terminal amino acid sequence: Xaa-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr, where Xaa consists of the following amino acid sequences: Thr, Val-Ala-Phe-Thr-, and Phe-Thr; and
> ii. the ability to inhibit the cytotoxic effect of TNF-α on murine A9 cells.

If the examiner refuses to consider claim 68 to be patentable to applicant, then it is believed that the count of the interference should be as follows, based on the broadest claim of the issued patent and the claim of the present application suggested by the examiner:

> A purified and isolated TNFα-binding protein which has a molecular weight of about 42,000 daltons and has at the N terminus the amino acid sequence
>
> Xaa Thr Pro Tyr Ala Pro Glu Pro Gly Ser
> Thr Cys Arg Leu Arg Glu
>
> where Xaa is hydrogen, a phenylalanine residue (Phe) or the amino acid sequences Ala Phe, Val Ala Phe, Gln Val Ala Phe, Ala Gln Val Ala Phe, Pro Ala Gln Val Ala Phe or Leu Pro Ala Gln Val Ala Phe
> or
> an isolated and purified Tumor Necrosis Factor

(TNF) binding protein (TBPII) having the following characteristics:

i. an N-terminal amino acid sequence: Xaa-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr, where Xaa consists of the following amino acid sequences: Thr, Val-Ala-Phe-Thr-, and Phe-Thr;

ii. the ability to inhibit the cytotoxic effect of TNF-α on murine A9 cells; and

iii. a molecular weight of about 30kd in reducing SDS-PAGE analysis.

In accordance with 37 C.F.R. §1.605(b), as the suggested claim of the examiner has been timely presented, it is requested that *ex parte* proceedings in this application be stayed pending a determination whether an interference will be declared, and it is further urged that such an interference be promptly declared in order to resolve all priority and patentability issues with respect to the present invention.

Respectfully submitted,

BROWDY AND NEIMARK
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UNITED STATES DEPARTMENT OF COMMERCE
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Applicants: Wallach et al.
Serial No.: 07/930,443
Filed: August 19, 1992
For: TUMOR NECROSIS FACTOR BINDING PROTEIN II, ITS PURIFICATION AND ANTIBODIES THERETO
Accorded Benefit of: U.S. Ser. No. 07/524,263, filed 05/16/90; Israel - 90339, filed 05/18/89, 91229, filed 08/06/89, 94039, filed 04/06/90

The case referred to above has been forwarded to the Board of Patent Appeals and Interferences because it is adjudged to interfere with other cases hereafter specified. Attention is directed to the fact that this interference is declared pursuant to 37 CFR 1.601 et seq., effective February 11, 1985 (49 F.R. 48416. 1050 O.G. 385). The interference is designated as No. 103,625.

By direction of the Commissioner of Patents and Trademarks and as required by 35 USC 135(c), notice is hereby given the parties of the requirement of the law for filing in the Patent and Trademark Office a copy of any agreement "in connection with or in contemplation of the termination of the interference."

The cases involved in this interference are:

Junior Party

Applicants: David Wallach, Hartmut Engelmann, Dan Aderka, Daniela Novick, Menachem Rubinstein,

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Serial No.: 07/930,443, filed August 19, 1992

For: TUMOR NECROSIS FACTOR BINDING PROTEIN II, ITS PURIFICATION AND ANTIBODIES THERETO

Assignee: None

Attorneys of Record: Alvin Browdy, Roger L. Browdy, Anne M. Kornbau, Ronald R. Snider, Norman J. Latker, Sheridan Neimark, A. Fred Starobin, Jerome J. Norris, Iver P. Cooper and John E. Tarcza

Associate Attorney: None

Accorded Benefit of: U.S. Ser. No. 07/524,263, filed 05/16/90; Israel - 90339, filed 05/18/89, 91229, filed 08/06/89, 94039, filed 04/06/90

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Serial No.: 07/768,443, filed 09/26/91, now Patent No. 5,344,915, granted 09/06/94

For: NOVEL PROTEINS AND THE PREPARATION THEREOF

Assignee: BASF Aktiengesellschaft

Attorneys of Record: Herbert B. Keil and Russell E. Weinkauf,

Associate Attorneys: None

Accorded Benefit of: PCT - PCT/EP90/00719, filed 05/04/90

Address: Keil & Weinkauf
1101 Connecticut Avenue, N.W.
Washington, DC 20036

Count 1

a) An isolated and purified Tumor Necrosis Factor (TNF) binding protein (TBPII) having the following characteristics:

i. an N-terminal amino acid sequence: Xaa-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr, where Xaa consists of the following amino acid sequences: Thr, Val-Ala-Phe-Thr-, and Phe-Thr;

ii. the ability to inhibit the cytotoxic effect of TNF-α on murine A9 cells;

iii. a molecular weight of about 30kd in reducing SDS-PAGE analysis.

or

b) A purified and isolated TNFα-binding protein which has a molecular weight of about 42,000 daltons and has at the N terminus the amino acid sequence

Xaa-Thr-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr-Cys-Arg-Leu-Arg-Glu

where Xaa is hydrogen, a phenylalanine residue (Phe) or the amino acids sequences Ala-Phe, Val-Ala-Phe, Gln-Val-Ala-Phe, Ala-Gln-Val-Ala-Phe, Pro-Ala-Gln-Val-Ala-Phe or Leu-Pro-Ala-Gln-Val-Ala-Phe.

The claims of the parties which correspond to this count are:

Wallach et al.: Claims 33, 34, 36-41, 44-46, 62, 65-68.

LeMaire et al.: Claims 1-3.

Mary F. Downey

Mary F. Downey
Administrative Patent Judge
(703) 308-7979

MFD/raj

...0-(Rev. 9-27-95) INTERFERENCE INITIAL MEMORANDUM

...ARD OF PATENT APPEALS AND INTERFERENCES: An interference is found to exist between the following cases

This interference involves 2 parties

PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
LeMaire et al	07/768,443	9/26/91	5,344,915	9/6/94

...plication has been patented, have maintenance fees been paid? N/A ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
PCT	PCT/EP90/00749	5/4/90	—	—
~~Germany~~	P3915672.0	5/9/89	—	—
~~Germany~~	P3922694.3	7/5/89	—	—

The claim(s) of this party which correspond(s) to this count is(are):

PATENTABLE CLAIMS: 1-3 — UNPATENTABLE CLAIMS: N/A

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTABLE CLAIMS: N/A — UNPATENTABLE CLAIMS: N/A

MAILED

OCT 01 1996

PAT. & T.M. OFFICE
BOARD OF PATENT APPEALS
AND INTERFERENCES

PARTY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Wallach et al	07/930,443	8/19/92		

If application has been patented, have maintenance fees been paid? N/A ___Yes ___No ___Maintenance fees not due yet

**Accorded the benefit of:

COUNTRY	SERIAL NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
US	07/524,263 FWC	5/16/90		
ISRAEL	90339	5/18/89		
ISRAEL	91229	8/6/89		
ISRAEL	94039	4/6/90		

The claim(s) of this party which correspond(s) to this count is(are):

PATENTABLE CLAIMS: 67 ~~6-11~~ — UNPATENTABLE CLAIMS: 33, 34, 36-41, 62, 68, 44-46, 65-66

The claim(s) of this party which does(do) not correspond to this count is(are):

PATENTABLE CLAIMS: NONE - — UNPATENTABLE CLAIMS: 47-59 42 43 63, 64

Instructions

1. For every patent involved in the interference, check if the fees have been paid by contacting the MAINTENANCE FEE DEPARTMENT at 308-5069. If fees are due and they have not been paid, the interference cannot be declared since it would involve an expired patent (35 USC 135(a); 37 CFR 1.606).
2. For each party, separately identify the patentable and unpatentable claims which correspond to the count. (37 CFR 1.601 (f), 1.601 (n), 1.609(b)(2)).
3. For each party, separately identify the patentable and unpatentable claims which do not correspond to the count (37 CFR 1.609(b)(3)).
4. Forward all files including those the benefit of which is being accorded.
5. Keep a copy of the Interference Initial Memorandum and any attachments for your records.

All information requested below must be attached on (a) separate sheet(s) and type-written.

6. On a separate sheet, set forth a single proposed interference count. If any claim of any party is exactly the same word for word as this count, please indicate the party, application or patent number, and the claim number.
7. For each claim designated as corresponding to the count, provide an explanation of why each claim defines the same patentable invention (37 CFR 1.609(b)(2)).
8. For each claim designated as not corresponding to the count, provide an explanation of why each claim defines a separate patentable invention (37 CFR 1.609(b)(3)).
9. For each additional count, if any, repeat steps 2-6 and, additionally, provide an explanation why each count represents a separate patentable invention from every other count (37 CFR 1.609(b)(1)).

DATE	PRIMARY EXAMINER (Signature)	TELEPHONE NO.	ART UNIT
2/15/96	Marian C. Knode	308-4311	1806
	GROUP DIRECTOR SIGNATURE (if required)		

**The serial number and filing date of each application the benefit of which is intended to be accorded must be listed. It is not sufficient to merely list the earliest application if there are intervening applications necessary for continuity.

THIS PAGE CAN BE DUPLICATED IF THERE ARE MORE THAN TWO INTERFERING PARTIES.

Page ___ of ___

EXPLANATION UNDER 37 C.F.R. 1.609 (b)2/3 FOR 07/930,443

1.609(b)2:

Wallach *et al.* (07/930,443)

Claims 33,34, 36-41, 62, 67, and 68 all define the same basic product through a wide variety of possible formats. However, whatever the format, the claims merely recite the same basic product. That product is a TNF binding protein having a particular N-terminal sequence. The reason 67 is designated as allowable is based on the critical molecular weight limitation which insures that the claim is drawn to the full length protein, not all active fractions, fragments, *etc.*. These fragments *etc.* are not enabled. Claims 38 and 41 recite a product in a product by process fashion while the other claims merely recited different structural features of the invention. Therefore, the claims do not define a structurally distinct product.

LeMaire *et al.* (5,344,915)

Claims 1-3 of the Lemaire patent (5,344,915) all correspond to the same protein product claimed by Wallach *et al.* The '915 application discloses that the N-terminal sequences of TNF receptor has a variant sequence. Note that some of the sequences overlap between the two claims. Noticeably, the sequence Val-Ala-Phe-Thr and the sequence Thr in the top part of the count correspond between the '915 patent and the Wallach application.

1.609(b)3:

Claims 47-55 are distinct in that these claims recite the antibody to the claims

recited above. Since the antibody has a distinct structure as represented by a separate amino acid sequence, it is not considered to be the same invention as that encompassed by the claims corresponding to the count of interference. Claims 56-59 are designated as not corresponding to the count because they are methods of using the antibodies of claims 47-55. Therefore, claims 47-59 represent a distinct invention from claims 33, 34, 36-41, 62, and 67-68.

The Lemaire patent does not contain any claims which do not correspond to the count.